

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

## PCT

To:

see form PCT/ISA/220

### WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/EP2004/011619

International filing date (day/month/year)  
14.10.2004

Priority date (day/month/year)  
15.10.2003

International Patent Classification (IPC) or both national classification and IPC  
C07D295/18, C07D257/04, C07D263/32, C07D213/81, C07D237/08, C07D239/26, C07D231/14, C07D241/12,

Applicant  
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- ☐ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material:  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing:  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 7

because:

☒ the said international application, or the said claims Nos. 7 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

**(III)**

Claim 7 is directed to a method of treatment of the human/animal body and therefore no preliminary examination is required (Rule 67.1(iv) PCT).

Moreover, it is noted by the IPEA that for the assessment of Claim 7 on the question whether its subject-matter is industrially applicable, no unified criteria exist in the PCT. The patentability under national patent laws can also be dependent on the formulation of the claims. The EPO, e.g., does not recognize the subject-matter of claims to the use of a compound in medical treatment as being industrially applicable, but will allow, however, claims to a known compound for the manufacture of a medicament for a new medical treatment.

**(V)**

Having regard to the International Search Report as well as the prior art cited by the Applicant in the description the present compounds of formula (I) differ from the disclosure in (D1) WO02/12190; (D2) WO03/024967; (D3) WO03/066604; (D4) WO2004/035556 due to the definition of present 1-/4-substituents on the diazepine moiety and/or substituents thereof.

The requirements of Art.33(2) PCT appear to be fulfilled.

It is noted that the publication number of the cited document WO03/00480 on p.1, l.7 of the description appears to be wrong.

The problem underlying the present invention appears to be the provision of novel compounds of formula (I) having selective histamine H3 receptor (ant-)agonistic affinity. (D1) and (D3) disclose compounds having similar properties. (D1), in particular Ex.50 therein, bears a benzyl instead of a benzoyl group and a 4-methyl substituent compared with present R1; (D3) discloses 4N-cycloalkyl, 1N(hetero-)aryl substituted piperazine derivatives, having no directly N-bound benzoyl group present. Moreover, although P-document (D4) is not relevant at this stage, it is noted that Ex.449-453 therein differ due to present R1/R3 substituents. (D1)/(D3) comprise structurally essentially different compounds and therefore they have not been taken into consideration in this respect. The Applicant has substantiated the claimed activity per se. Accordingly an inventive step can be acknowledged, provided that all claimed compounds show selective H3-receptor (ant-)agonistic properties. In this connection reference is made to the broad substituents' definitions "(hetero-)aryl; heterocyclyl;", appearing in the claims without the specified definition given on p.3 of the description.

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**Box No. V    Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-8
	No: Claims	
Inventive step (IS)	Yes: Claims	1-8
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-6, 8
	No: Claims	7

2. Citations and explanations

see separate sheet